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Full Length Article

The pattern of infection and antibiotics use in terminal cancer patients

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KEYWORDS

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Abstract *Background:* Although cancer patients are susceptible to infection, there is no evidence-based published guideline on the appropriate use of antimicrobial treatment in this group of patients.

Methods: We retrospectively collected medical records of all terminal cancer patients who died in the oncology department over a 15-month period and were reviewed for the pattern of infection and causes of antimicrobial use during the patients' last admission of life.

Results: A total of 258 eligible patients were enrolled, there was an equal distribution of males and females (M/F: 129/129), and the mean age was 60.5 years. 221 patients admitted with fever (85%), 22 patients (8.5%) got fever after hospitalization and 15 patients (5.8%) did not suffer from fever. Among patients with fever, 46 patients (18.9%) had two infection episodes and 197 patients (81.1%) had only one infection episode. The culture results revealed positive in 98 patients (40%) with gram-negative organisms were the dominant organisms. The major infection sites were the respiratory tract, urinary tract and wound. 114 patients (47%) received one antibiotic and 129 patients (53%) received more than one. The mean duration of hospitalization was significantly longer for infected patients than for uninfected patients (8.00 vs. 18.15 days, $p = 0.0001$). Outcome of antibiotic use revealed 42 patients (17.3%) with symptoms improved 71 patients (29.2%) with stationary symptoms and 130 patients (53.5%) revealed symptom deterioration.

Conclusions: Our study revealed that antibiotic therapy for terminal cancer patients should be on a clear rationale. We need further study to clarify if there is survival effect with antibiotic use or not.

Introduction

Various factors either disease-related or therapy-induced make cancer patients more susceptible to infections rather than normal persons. Most cancer patients have many symptoms that

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not only cause discomfort, but also impact quality of life. Although there are different symptoms depending on the type of cancer, the most common symptoms include pain, fatigue, dyspnea, nausea, vomiting, constipation, and altered mental status [1–3]. Because one of the most important goals of medical practitioners is to alleviate suffering and improve the quality of life, many efforts and studies have focused on symptom management and control in cancer patients [4]. Among those factors which cause discomfort, infection is responsible for substantial patient distress and adverse symptoms.

Infection in cancer patients has been widely reported, but very few studies have focused on the infection and its management in palliative care patients [5–9]. However, the extent of benefit and optimal antibiotic use in cancer patients who are receiving palliative care, especially in their end-of-life period, was still not well-documented, and certain controversies remained unsettled [10].

We conducted a retrospective study in the King Abdullah Medical City-Holy Capital; a Saudi Tertiary Care hospital to investigate the pattern of infection and antibiotic use in those special type of patients.

Materials and methods

The current retrospective study included 258 terminal cancer patients who died in the oncology department under palliative care in the King Abdullah Medical City-Holy Capital (KAMC-HC) during the period from October 2010 to December 2012. Eligibility criteria were;

- Pathological diagnosis of cancer.
- Evidence of advanced disease beyond cure.
- Death during hospitalization at KAMC-HC.

We recorded the demographic data of patients, including sex, age, cancer diagnosis, and hospitalization durations at the oncology ward. According to status on admission all patients were assigned to one of three strata: infection-admit, new-infection and infection-free. When infection was identified, we recorded the date of infection and infection-related information including the symptoms/signs associated with infection, infection focus, bacteriological culture and the pathogen results. When antibiotics were employed, we also recorded the period of use. After the course of antibiotic use was completed, we evaluated whether the initial infection-related symptoms/signs had or had not improved.

Infection was defined as the presence of symptoms or physical signs that were interpreted and assessed by the attending physicians to have been caused by a microbial agent. We considered infection developed after 72 h from admission as nosocomial infections [11,12].

Statistical methods

Data collected were analyzed using SPSS computer software Continuous variables were summarized as mean and standard deviation or median and range as appropriate. Categorical data were presented as frequencies and percentages. Significance was defined as a P-value of <0.05.

Ethical consideration

Ethical approval to conduct the study was sought from the IRB review committee before the commencement of the study.

Results

Patient characteristics

During the study period, a total of 258 patients with advanced cancer were enrolled into the palliative care service and involved in our study. Among those patients, the male to female sex distribution was 1:1 (129/129). The mean age was 60.5 (S.D. ± 15.6 ranging from 17 to 101).

221 patients (85.7%), admitted by fever, 22 patients (8.5%) had got fever during the admission period; after 72 h from admission and 15 patients (5.8%) were admitted and died without fever or antibiotic. Among patients with fever, 46 patients (18.9%) had two infection episodes during the same hospitalization period, and 197 patients (81.1%) had only one infection episode. The common cancer types included colorectal cancer, breast cancer, lung cancer and biliary system (liver and biliary tract) Table 1.

Major symptoms and outcome after antibiotic use

For major symptoms represented by the patients and outcome; check Table 2.

Infection characteristics

The major infection sites were the respiratory tract, urinary tract and wound. Among the patient's infective episodes; the bacteriological culture results were positive in 98 patients (40%) and negative in 145 patients (60%). The gram –negative organisms were the dominant organisms (gram-negative vs. gram-positive; 64 vs. 22) Table 3.

Causes of antibiotic use

All the patients with infective episodes in our study were treated with antibiotics (100%) and continued till death. 114 patients (47%) received one antibiotic and 129 patients (53%) received more than one. Ceftriaxone was the most commonly prescribed antibiotic, received by 81 patients (33.3%), and followed by piperacillin/tazobactam received by 37 patients (15.2%) Table 4.

Duration of hospitalization

The median duration of hospitalization among the 258 patients who were enrolled into the palliative care service and involved in our study was 14.5 days (ranging from 1 to 159 days), the other 15 non infected patients had a median hospitalized duration of 5 days (ranging from 1 to 32 days).

For the 197 patients who had one infection episode, the median hospitalized duration was 13 days (ranging from 1 to 159 days). Additionally, the 46 patients who had two episodes had a median duration of hospitalization of 22 days (ranging

Table 1 Patient's characteristics.

	Numbers	Percentage %
Sex		
Male	129	50
Female	129	50
Total	258	50
Age		
Mean	60.5	
Standard deviation	±15.6	
Range (minimum – maximum)	17–101	
Status on admission		
Fever on admission	221	85.7
*Get fever after admission	22	8.5
No fever at all	15	5.8
Total	258	100
Infection episodes		
Once	197	81.1
Twice	46	18.9
Total	243	100
Primary cancer site		
Colo- rectal	36	14
Breast	24	9.3
Biliary system	17	6.6
Sarcoma	9	3.5
Genitor-urinary	20	7.8
HCC**	20	7.8
Lung	22	8.5
Pancreas	17	6.6
H&N***	9	3.5
CUP****	12	4.7
Lymphomas and leukaemias	41	15.9
Stomach	9	305
Others	22	8.2
Total	258	100

* After 72 h from admission.
** Hepatocellular carcinoma.
*** Head and neck.
**** Cancer of unknown primary.

Table 2 Major symptoms and outcome after antibiotic use.

Major symptoms	Frequency (TN* 243)		Improvement	
	Number	(%)	Number	(%)
Pain	155	(63.8)	31	12.8
Dyspnea	142	(58.4)	9	3.7
Delirium	77	(31.7)	0	0
Anxiety	48	(19.8)	0	0
Weakness	100	(41)	2	0.8
Total out come				
Improved	42		17.3	
Static	71		29.2	
Deteriorated	130		53.5	

* TN; total number of patients.

from 2 to 90 days). For those 221 patients who were admitted with infection, their median duration of hospitalization was 14 days (ranging 1–107 days), and for the 22 patients who suffered new infection during the admission period, their median duration of hospitalization was 23.5 days (ranging from 155 days 4–159 days). The differences seen in hospitalized days between infected and non-infected patients and between who got fever twice and once were highly significant ($p < 0.001$, 0.001 respectively) Table 5.

Discussion

Palliative care is specialized medical care for people with serious illnesses. It is focused on providing patients with relief from the symptoms, pain and stress of a serious illness — whatever the prognosis. The goal is to improve quality of life for both the patient and the family as they are the central system for care. End-of-life care provides physical, mental, and emotional comfort to people who are living with and dying of advanced illness [13]. The use of antimicrobials controlled symptoms in the majority of the urinary tract infections, but were less effective in controlling symptoms in the other sites of infection [14].

Terminal cancer patients are highly susceptible to infections due to a variety of causes such as concurrent debilities, asthenia, decreased level of consciousness, immobility, deteriorated nutritional and immune status when patients were close to end of life.

In our study, in non neutropenic terminally ill cancer patients, the total infection rate was 243 patients (94.2%); 221 patients (85.7%) admitted with infection and 22 patients (8.5%) had got fever during the last admission period prior to death with 46 patients (18.9%) having two infection episodes. This result is higher than that recorded in other studies ranging from 63% to 87% [15–17]. This difference may be explained by the variation in populations, study areas, care facilities and the definition of infection.

The most frequent site of infection in our patients was respiratory (48.6%), followed by urinary tract (12.3%) and wound (4.1%). This results is corresponding to the study done by Lam at 2005 [18], but different from the studies of Vitetta et al. [19] Homsi et al.,[20] and Pereira et al. [21].

Although there are many clinical studies [22–24] that have examined the safety and feasibility of oral antibiotics, still the parenteral route is the main used one. In our study; among the patients who received antibiotics, 98 patients (40%) received antibiotics based on cultures and sensitivity and 87.2% of them used antibiotics through the parenteral route, which can be explained by many factors such as poor general condition of our patients which may affect on the swallowing, the severity of infection and the physician's own decision.

As we saw in our study; all patients with infective episodes received antibiotics, which reflect the high prevalence of their usages. We believe that the antibiotic use in patients under palliative care even in their end of life days is fairly common practice. This can be explained by many reasons; firstly, many patients were cared by medical oncologists with less experience in palliative care so they chose aggressive treatment rather than observation or symptom control. Second, still the patients and their families prefer aggressive treatment by antibiotics even with expected minimal out come. Third, many physicians considered the use of antibiotic with the potential to postpone the patient death. Fourth, the concept of antibiotic usage as a part of usual care may give some symbolic comfort for patients and their care givers. Lastly, in our center, before accepting any case under palliative care, we routinely meet patients and their family to explain the positive concept of palliative

Table 3 Infection characteristics.

Major sites of infection	Frequency total number (243)	Percentage %
Respiratory tract	118	48.6
Urinary tract	30	12.3
Wound	10	4.1
Bacteriological results		
Positive cultures	98	40
Negative cultures	145	60
Classification of organisms		
Gram −ve	64	26
Gram +ve	22	9
Mixed	12	4.9
Total number	98	100

Table 4 Pattern of antibiotic use.

	Frequency total number (243)	Percentage %
Antibiotic utilization pattern		
Empirical	145	60
Based on culture and sensitivity	98	40
Administration route		
Parenteral	212	87.2
Enteral	16	6.6
Both	15	6.2
Patients on antibiotics		
One	114	47
More than one	129	53

Table 5 Infection and duration of hospitalization.

Variable	Number (patient)	median	Range (days) (minimum −maximum)	*p*-Value
Total	258	14.5	158 (1–159)	
Infection				
No	15	5	31 (1–32)	
Yes	243			
Once	197	13	158 (1–159)	0.001
Twice	46	22	88 (2–90)	
Admitted with infection	221	14	106 (1–107)	
Get infection while admission	22	23.5	155 (4–159)	$p < 0.001$

P-value < 0.05

care, but unfortunately not antibiotic use, as we did not know when we start and end antibiotic administration.

The use of antibiotics on terminal cancer patients at the end of life for symptomatic improvement is still questionable; few studies support the use of it [25–27], while many studies are considered futile [19,28–32].

In the prospective report by Vitetta et al. [19], 37 patients with 42 separate infection events were noted from 102 consecutive admitted terminal patients in a hospice ward and after antibiotics were administered, the extent of symptom control approached at least 40%. This study suggested that appropriate antibiotic use as infection therapy provided benefits for symptom control in terminal cancer patients. On the contrary, in reports by Oh et al. [21], antibiotics were used on 119 patients among a total of 141 admitted terminal cancer patients. In that study, only 15.1% of the patients had infectious symptom improvement and more than half (55.4%) did not have any benefit what so ever. In our study; after antibiotic use, 42 patients (17.3%) had symptom improvement, 71 patients (29.2%) had stationary symptoms and 130 patients revealed symptom deterioration. The duration of hospitalization was more prolonged in patients with infection in comparison to patients without infection, especially for those who had got infection during the hospitalization period and for whom suffered from more than one episode.

The symptomatic treatment in advanced cancer patients at end of life in the form of pain, fever and dyspnea with opioids and antipyretics remain effective means but the prolonged life

span in those particular types of patients remained unclear [33–35].

Limitation

There are two main limitations to our study, firstly; the heterogeneity of the sample as regards cancer diagnosis (hematology vs. solid tumors). The second limitation was the retrospective nature of the study which depends totally on medical documentation of diagnosis, symptom severity and their response, and other outcome measures. Also the variation in the choice of antibiotic even within the same site of infection among different physicians.

Conclusions

The use of antibiotics in patients with advanced cancer near their end of life is a common practice in our center. We must know that antibiotics are not safe medications and had a long list of potential adverse effects with increasing risk of antimicrobial resistance besides the significant cost. So we need further prospective studies to identify several factors such as the origins of infection, performance status, and laboratory data are that necessary to help in create guidelines or protocols to effectively choose the most suitable patients and appropriate antibiotic therapies.

Conflict of interest

The authors certify that there is no actual or potential conflict of interest in relation to this article.

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